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Intrauterine, postpartum and adult relationships between arachidonic acid (AA) and docosahexaenoic acid (DHA)

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ABSTRACT

Erythrocyte (RBC) fatty acid compositions from populations with stable dietary habits but large variations in RBC-arachidonic (AA) and RBC-docosahexaenoic acid (DHA) provided us with insight into relationships between DHA and AA. It also enabled us to estimate the maternal RBC-DHA (mRBC-DHA) status that corresponded with no decrease in mRBC-DHA during pregnancy, or in infant (i) RBC-DHA or mRBC-DHA during the first 3 months postpartum (DHA-equilibrium) while exclusively breastfeeding. At delivery, iRBC-AA is uniformly high and independent of mRBC-AA. Infants born to mothers with low RBC-DHA exhibit higher, but infants born to mothers with high RBC-DHA exhibit lower RBC-DHA than their mothers. This switch from 'biomagnification' into 'bioattenuation' occurs at 6 g% mRBC-DHA. At 6 g%, mRBC-DHA is stable throughout pregnancy, corresponds with postpartum infant DHA-equilibrium of 6 and 0.4 g% DHA in mature milk, but results in postpartum depletion of mRBC-DHA to 5 g%. Postpartum maternal DHA-equilibrium is reached at 8 g% mRBC-DHA, corresponding with 1 g% DHA in mature milk and 7 g% iRBC-DHA at delivery that increases to 8 g% during lactation. This 8 g% RBC-DHA concurs with the lowest risks of cardiovascular and psychiatric diseases in adults. RBC-data from 1866 infants, males and (non-)pregnant females indicated AA vs. DHA synergism at low RBC-DHA, but antagonism at high RBC-DHA. These data, together with high intakes of AA and DHA from our Paleolithic diet, suggest that bioattenuation of DHA during pregnancy and postnatal antagonism between AA and DHA are the physiological standard for humans across the life cycle.

1. Introduction

The long-chain polyunsaturated fatty acids (LCP) docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and arachidonic acid (AA) are structural components of membrane phospholipids (PL), modulators of gene expression and precursors of eicosanoids (AA, EPA), resolvins (AA, EPA, DHA) and (neuro)protectins (DHA) [1]. DHA and AA are notably abundant in the central nervous system and play important roles in fetal and infant neurodevelopment [2]. Low status of LCP, notably LCPω3, is also intimately related to cardiovascular and psychiatric diseases at adult age [3]. Most Western countries are characterized by low intakes of LCPω3 (especially EPA and DHA), which contrasts with the evolution of our ancestors in a land–water ecosystem with abundantly available LCPω3 and LCPω6 (especially AA) [4–9]. Higher LCP in circulating cord plasma lipids compared with maternal plasma [named 'biomagnification'[10]] and the loss of maternal DHA during lactation [11] might be indicative for a low LCPω3 status in Western countries [8].

Pregnant and lactating women have higher LCP needs [12] to support the development of the fetus and infant. This is notably the case for DHA, which becomes synthesized from ALA with difficulty [13,14]. Infants accrete AA in their brains especially in early pregnancy, while DHA accretes rapidly from week 30 of pregnancy to 2 years postpartum [15–20]. Transfer of LCP during pregnancy and lactation occurs at the expense of the mother and the resulting depletion of maternal stores during lactation has been named the 'maternal depletion syndrome' [21,22]. Maternal LCP depletion may especially occur at longer gestation [23], short birth intervals, increasing parity and twin pregnancies [24–26]. Postpartum maternal LCP depletion seems notably to affect DHA, and not AA. While AA in maternal plasma phospholipids (PL) and erythrocytes (RBC) increases to prepregnancy values after delivery, there is a highly consistent postpartum decrease of maternal plasma PL- and RBC-DHA in lactating compared to non-lactating women [11,27]. A number of studies have demonstrated that a low intake of LCPω3 during pregnancy results in slightly shorter gestation, marginally lower birth weight and increased risk of preterm delivery [28]. A low maternal DHA status, as encountered in populations with low seafood consumption, has also been associated with a higher incidence of postpartum depression [29,30]. The causality is however uncertain, since randomized

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controlled trials (RCTs) with DHA in pregnancy and lactation have been inconclusive [31–35]. Finally, a declining maternal DHA status during pregnancy was suggested to be involved in compromised maternal selective attention, which is a key component of cognition [36]. Other RCTs aimed at improvement of infant neurodevelopment by supplementation of pregnant women or their infants with LCP [37]. These maternal DHA supplementation studies show at most subtle effects [38–42], which is in line with meta-analyses of postnatal LCP supplementation of formula milk for preterm and term infants [43,44]. However, two large recent trials that were not yet included in the meta-analyses, reported positive influences on infant visual acuity [45,46]. The outcomes of RCTs and meta-analyses contrast with the positive relations between neonatal brain DHA and cognitive and behavioral performance that are noted in the combined human and animal studies [2].

We present an integrated overview of RBC-AA and DHA data, deriving from mothers and infants at delivery and after 3 months of exclusive lactation. RBC fatty acids (FA) are considered to be reliable parameters of long term dietary intakes [47], The samples were obtained from three tribes living in Tanzania. The study populations are characterized by life-time stable dietary intakes. Their intake of fish ranges from very low (mean 0 times/week; SD 0.7), to intermediate (3 ± 2 times/week) to high (5 ± 2 times/week) [48,49]. Their RBC-FA compositions provided us with insight into the perinatal relationships between maternal and infant DHA and AA status, and enabled us to estimate the maternal DHA status at which either the infant or its mother reaches a state of DHA equilibrium, which implies that there were no changes in RBC-DHA from delivery until 3 months lactation. We finally focused at the relationship between RBC-AA and RBC-DHA as derived from the many RBC data that we have collected during the past 20 years from populations with a wide range in RBC-DHA.

2. Intrauterine biomagnification of AA may aim at uniform fetal AA status

We found consistently higher AA in newborn umbilical cord blood RBC (in g/100 g; g% FA) as compared to the corresponding maternal RBC (Fig. 1). This 'biomagnification' of AA [10] was independent of maternal AA status at delivery and at 3 months postpartum (Fig. 2A and B). Biomagnification of AA is in line with data from many others who studied plasma PL-AA [27,50] or RBC-AA [51–53]. Higher infant RBC-AA than maternal RBC-AA was e.g. previously found by us in Dominica [54] and by Vlaardingenbroek and Hornstra in The Netherlands [53]. Most importantly however, we noticed a remarkably uniform, high infant RBC-AA at delivery (Fig. 1). This low inter-individual variation occurred despite the sizeable between-tribe differences of maternal RBC-AA and RBC-DHA (Fig. 3). Consequently, AA biomagnification seems to aim at a uniform infant AA status during pregnancy, rather than just causing higher AA in infants than in their mothers, which may emphasize the importance of a certain infant prenatal AA status. Intrauterine AA has been implicated in fetal growth [55,56], while AA also rapidly accretes in the fetal brain [16–20,57].

After delivery, maternal RBC-AA increased consistently during 3 months of exclusive breastfeeding (Fig. 1), possibly because of discontinued AA utilization by the placenta [58,59], discontinued transport to the fetus, or both. The maternal increase of AA status was accompanied by a drop in infant AA status, which might represent the transition of the infant's RBC-FA composition to adult proportions and coincides with the postpartum changes in the composition of the infant's RBC-PL species [60,61]. Mechanistically,

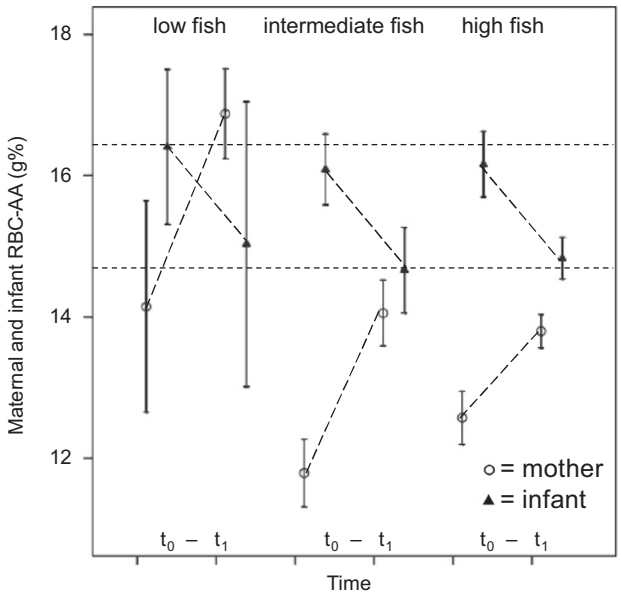

Fig. 1. Maternal (○) and infant (▲) RBC-AA at delivery and after 3 months lactation in mothers with low, intermediate or high fish intakes. Data are means (± 2 s.e.m.) of total RBC fatty acids (g%) at delivery (t_0) and 3 at months postpartum (t_1) for women with low fish intakes ($n=6$ at delivery; $n=7$ at 3 months PP) and their infants ($n=8$, 6), women with intermediate fish intakes ($n=27$, 38) and their infants ($n=29$, 38) and women with high fish intakes ($n=34$, 60) and their infants ($n=36$, 61).

the postnatal RBC-AA decrease might also result from the discontinued AA transport across the placenta and from the change of hormonal milieu that accompanies delivery. The latter is likely to influence FA enzymatic activities. It was e.g. shown that the infants' LCP-synthetic activity decreases drastically after delivery [14]. Even the relatively high milk AA contents in some of the Tanzanian tribes (0.37 g% in Maasai vs. 0.80 g% in the Pare-like Nyiramba [62]) were unable to prevent this decrease in infant RBC-AA. The rapid postnatal drop of infant RBC-AA raises the question whether milk AA is at all intended to sustain infant AA status after delivery. This suggestion is in line with Hsieh et al.[63], who recently showed that central nervous system (CNS) AA contents in baboon neonates are tightly controlled at the level of incorporation or utilization, that CNS AA levels were unaffected by (postnatal) dietary AA and decreased in all CNS structures with age. Taken together, a uniformly high infant AA status seems notably important during pregnancy, which contrasts with the predominant accretion of DHA in the infant's brain after birth.

3. Where DHA biomagnification turns into bioattenuation during pregnancy

Infants born to mothers with low and intermediate fish intakes and DHA status exhibited higher RBC-DHA contents as compared to their mothers (Fig. 3), which has been named 'biomagnification' [10]. However, in our study this biomagnification occurred only up to about 6 g% RBC-DHA (Fig. 4A). Beyond this turning point, infant RBC-DHA was mostly lower than maternal RBC-DHA, suggesting 'bioattenuation', rather than biomagnification. The previously published mean RBC-DHA values for the Dutch population (with low fish intakes) [53] and for the Dominican population (Caribbean Sea; with high fish intakes; [54]) proved highly consistent with the suggested mother–infant RBC-DHA relation at delivery. Bioattenuation has also been noticed in a maternal fish oil supplementation study conducted by Dunstan et al. [64], who referred to it as 'saturation'. The present information from

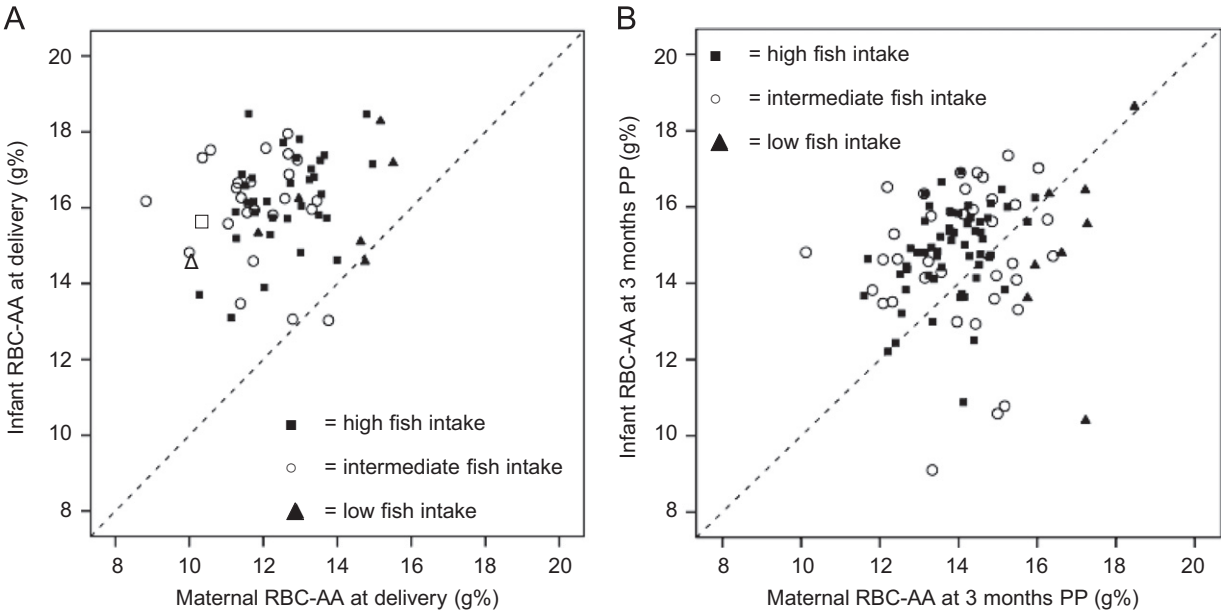

Fig. 2. Relations between maternal and infant RBC-AA at delivery (A) and after 3 mo lactation (B) for mother–infant pairs with low (▲, $n=6$), intermediate (○, $n=24$) and high (■, $n=33$) fish intakes. Mean data for Dominican ($n=7$; □) and Dutch ($n=183$; Δ) mother–infant couples are derived from Refs. [53,54], respectively. PP, postpartum, dotted line represents $y=x$ for 'equal AA sharing'.

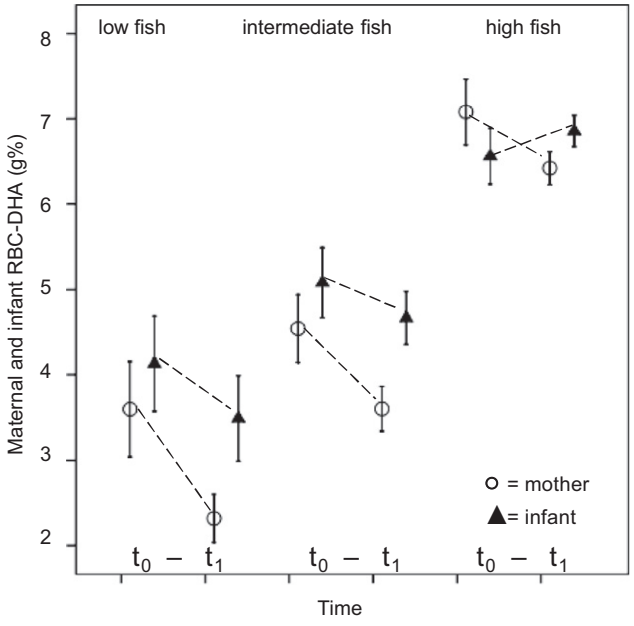

Fig. 3. Maternal (○) and infant (▲) RBC-DHA at delivery and after 3 months lactation in mothers with low, intermediate or high fish intakes. Data are means (±2 s.e.m.) of total RBC fatty acids (g%) at delivery (t_0) and 3 at months postpartum (t_1); for n, see Fig. 1.

populations with lifetime high fish-intakes suggests that DHA biomagnification is confined to the low maternal DHA status that is typically encountered in most Western countries.

4. Infant RBC-DHA equilibrium

The postpartum mother-to-infant DHA transfer via the milk was unable to prevent an RBC-DHA drop in the infants born to mothers with low and intermediate fish intakes, but did enable a postpartum RBC-DHA increase in infants from the mothers with high fish intakes (Fig. 3). Postpartum infant DHA equilibrium may therefore be reached at DHA intakes that are somewhat below those of our study group with an average fish intake of 5 times/week. Using the joined data of all mothers and infants we estimated that mothers with an RBC-DHA status of about 6 g% in early pregnancy will have an RBC-DHA of about 6 g% at delivery and will give birth to infants with about 6 g% RBC-DHA [48] (Fig. 4A). This 6 g% infant RBC-DHA will then remain constant during lactation, but the mother will under these circumstances lose DHA to reach a maternal RBC-DHA of about 5 g% after 3 months of exclusive lactation (Fig. 5A). Postnatal infant DHA equilibrium, i.e. a maternal RBC-DHA of 6 g% at delivery, goes along with a mature milk DHA level of about 0.4 g% (Kuipers, unpublished). The combination of a state of infant DHA-equilibrium and maternal DHA losses during lactation illustrates a postnatal DHA surge via the milk and can therefore be considered as a genuine form of postnatal DHA-biomagnification. We conclude that a maternal DHA status corresponding with an RBC-DHA status of 6 g% predicts a state of DHA equilibrium in her infant during 3 months postpartum.

5. Maternal RBC-DHA equilibrium

Maternal RBC-DHA was consistently lower after 3 months of lactation as compared to delivery, suggesting that the mothers were losing DHA to their infants via the milk (Fig. 3). However, although maternal RBC-DHA decreased in all groups, the decrease was lowest in mothers with the highest fish intakes (i.e. 5 times/week). This implies that maternal DHA equilibrium may occur at fish intakes that exceed those encountered by us in the population with the highest fish intakes. By extrapolating the data of our 3 Tanzanian groups, we estimated that this equilibrium may be reached at a maternal RBC-DHA at delivery of about 8 g% (Fig. 4B). This state of maternal postnatal DHA equilibrium corresponds with a maternal RBC-DHA status of 8 g% in early pregnancy [48], an infant RBC-DHA of about 7 g% at delivery that increases to 8 g% at 3 months postpartum and a mature milk content of about 1 g% DHA (Kuipers, unpublished) (Fig. 5B). We coined this lower infant RBC-DHA compared to maternal RBC-DHA bioattenuation [48].

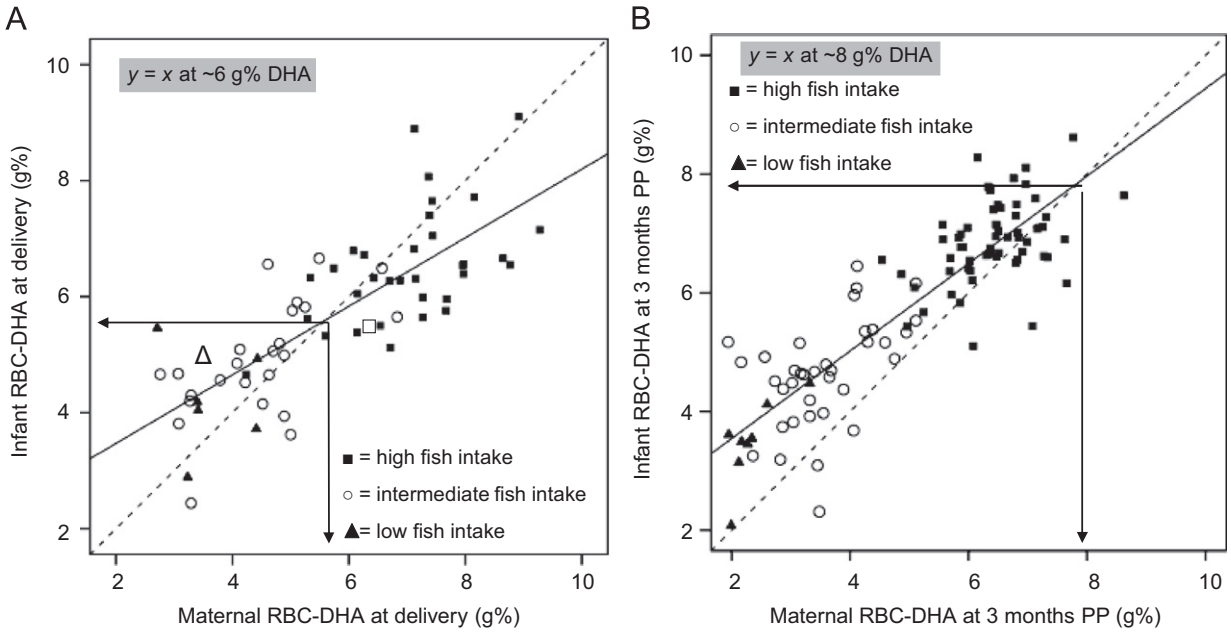

Fig. 4. Relations between maternal and infant RBC-DHA (in g%) at delivery (A) and after 3 months of lactation (B) for mother–infant pairs with low (▲, $n=6$), intermediate (○, $n=24$) and high (■, $n=33$) fish intakes. Dotted lines indicates $y=x$ for 'equal DHA sharing'. Data for Dominican ($n=7$; □) and Dutch ($n=183$; Δ) mother–infant pairs are derived from Refs. [53,54] respectively. The point of intersection of $y=x$ with the trend line $y=0.59+2.29$ ($R^2=0.61$; $p<0.001$) in Panel A is at an RBC-DHA of about 6 g%. The intersection of $y=x$ with the trend line $y=0.74+2.07$ ($R^2=0.76$; $p<0.001$) in Panel B is at an RBC-DHA of about 8 g%. Below these values, infants have generally higher DHA compared to their mothers (biomagnification); beyond these values infants have generally lower DHA compared to their mothers (bioattenuation). PP, postpartum.

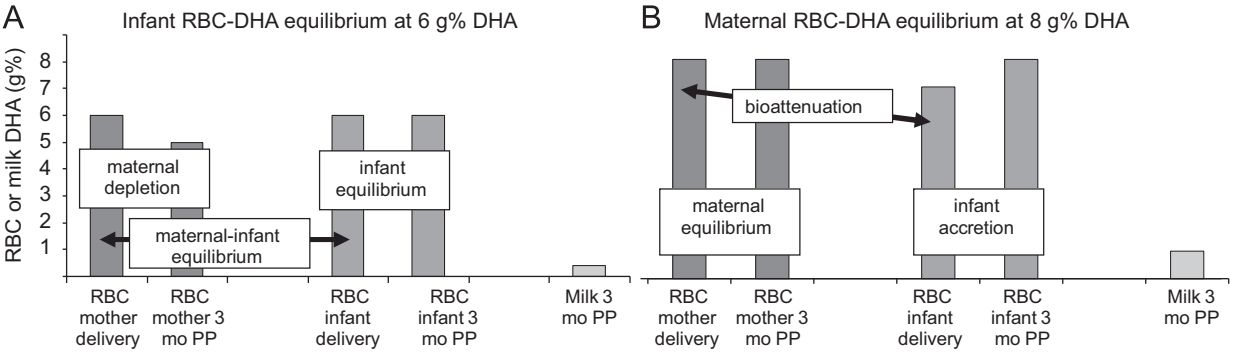

Fig. 5. Synoptic overview of the DHA contents of various maternal and infant compartments at infant (Panel A) and maternal (Panel B) RBC-DHA equilibrium from delivery to 3 months postpartum. Data represent medians for RBC-DHA and milk-DHA in g%. Panel A: infant RBC-DHA equilibrium from delivery to 3 months postpartum is reached at 6 g% infant RBC-DHA. This corresponds with a maternal RBC-DHA of 6 g% in early pregnancy, a maternal RBC-DHA of 5 g% after 3 months lactation and a mature milk DHA content of 0.4 g%. Mother and infant are at equilibrium at delivery, but the mother loses DHA during lactation. Panel B: maternal RBC-DHA equilibrium from delivery to 3 months postpartum is reached at 8 g% maternal RBC-DHA. This corresponds with an infant RBC-DHA of 7 g% in early pregnancy, an infant RBC-DHA of 8 g% after 3 months lactation and a mature milk DHA content of 1.0 g%. Infant RBC-DHA is lower than that of its mother at delivery (bioattenuation), but the infant reaches adult RBC-DHA contents within 3 months of lactation.

Despite this intrauterine bioattenuation, infant RBC-DHA increases rapidly to adult levels of about 8 g% during 3 months of lactation. Bioattenuation might illustrate the importance of limiting transplacental DHA transport at high maternal fish intakes, while the subsequent postnatal period is characterized by a mother-to-infant surge of DHA via the milk in all groups. This postpartum mother-to-infant DHA surge clearly occurs at the expense of the mother unless she had reached a steady state RBC-DHA of 8% or higher from high lifetime fish intakes. The postnatal DHA transfer from the mother to her infant coincides with a more rapid postnatal accretion of DHA in the infant brain, compared with AA [16–20,57] and may therefore illustrate the increasing importance of DHA for structural and other purposes notably after birth. Another function of the postnatal DHA-surge might be the rapid initiation of postnatal competition of DHA with AA in those organs that are sensitive to DHA vs. AA competition (see below).

6. What maternal DHA status is best?

The question arises as to what maternal DHA status is best for both the mother and her infant. At present, there is consensus on recommending an average DHA intake of at least 200 mg/day during pregnancy and lactation [28]. A number of studies have indicated that the intake of fish and fish oils during pregnancy result in slightly longer gestation, marginally higher birth weight and a reduced risk of preterm delivery [28]. However, little information can be derived from the current RCTs with DHA during pregnancy that targeted infant neurodevelopment.

The largest RCT so far with cod liver oil (1200 mg DHA/day) on top of a baseline diet containing 200–300 mg DHA/day by Helland et al. [40–42] showed no differences in cognitive development at 6 and 9 months, and a promising higher IQ at 4 years of age, but not at 7 years. They also found that neonates with mature EEG had higher DHA in umbilical plasma PL, compared with counterparts with less mature EEG [40]. A higher maternal plasma PL-DHA correlated with sequential processing, but milk-DHA did not correlate with IQ scores at 7 years [42]. These outcomes were in line with the negative outcomes for the associations between umbilical plasma PL- and RBC-DHA and infant cognitive development at 4 and 7 years in another study [38,39]. Additional studies, however, revealed that supplementation of pregnant women with fish oil might influence the infants' visual maturation and acuity [65–67] and newborn sleep pattern maturity [68]. Thus, results of maternal DHA supplementation studies show at most subtle effects, which is in line with the results of meta-analyses of postnatal LCP supplementation of formula milk for preterm and term infants [43,44]. Two recent large trials with postnatal DHA supplementation, however, again reported positive influences on infant visual acuity [45,46]. The outcomes of most RCTs contrast with the positive relations between neonatal brain DHA and cognitive and behavioral performance that are noted in the combined human and animal studies [2]. The discrepancy might relate with e.g. differences in frequencies of polymorphisms in the desaturase enzymes and the lack of dose-adjustment to differences in the individual baseline maternal and infant DHA status. Another factor might be the relatively short-term supplementation of low doses of DHA that are not able to cause a stable high maternal and infant DHA status, which is needed to arrive at beneficial effects of DHA. Therefore, from the perspective of infant neurodevelopment, the question remains currently unresolved and may need a broader view that takes into account studies of relationships between adult DHA status and functional outcomes.

High milk and RBC-DHA contents are in line with the optimal RBC-DHA status as proposed for the prevention of psychiatric and cardiovascular diseases at adult age. Epidemiological studies have linked high fish consumption, EPA+DHA intakes or EPA+DHA status, to a reduction in affective disorders [69], cognitive impairment [70], Alzheimers disease [71] and postpartum depression [29]. An RBC-(EPA+DHA) $\geq$ 8 g%, also named the omega-3 index, as found in healthy subjects in Japan, seems an appropriate target to minimize major depressive disorders and bipolar depression [69]. Meta-analyses of RCTs are positive, but heterogeneous, for depression [72,73], positive for cognitive impairment [74], but negative for Alzheimer's disease [75]. The relation between LCPω3 and postpartum depression has not been substantiated by RCTs [31–35], but none of these studies concomitantly investigated the course of RBC-DHA as a proxy of the maternal depletion syndrome. A more consistent picture emerges from studies between the relation of LCPω3 with cardiovascular disease. For example, the study by Helland et al. [40–42] showed a lower cholesterol/HDL-cholesterol ratio in the women supplemented with cod liver, compared to corn oil [76]. Various RCTs in notably secondary prevention of cardiovascular disease have indicated the beneficial effects of LCPω3 supplementation [77,78]. These have led to the advice of at least 2 times fish per week (about 450 mg LCPω3/day) for the general population and an intake of 1 g EPA+DHA for those with cardiovascular disease [79]. There is evidence that daily LCPω3 intakes $>$ 450 mg are beneficial for the lowering of heart rate, blood pressure and triglycerides and to reach maximum antithrombotic effects [80]. Subjects with RBC-DHA $>$ 8 g% (omega-3 index $>$ 10 g%) may reach the lowest risk for acute coronary syndrome and sudden cardiac death [81–85].

High milk DHA and RBC-DHA contents also comply with the high intakes of EPA and DHA, as calculated from the presumed diet of our Paleolithic ancestors [7,8]. These are likely to have evolved in a water–land ecosystem in East-Africa [4–9], where the fossil record indicates that they exploited aquatic resources. It is therefore likely that our genome has, especially during the about 2.5 millions years of evolution since *homo erectus,* become adapted to a diet [86,87] that was rich in LCPω3 and LCPω6 from our aquatic niche. The presumed high DHA intakes by our ancestors are likely to have resulted in maternal stores that prevented depletion during lactation and sustained a stable DHA transfer to the developing infant, where DHA plays an important role in the maturation of the brain [20], retina [88] and other central nervous structures [63]. Taken together, our finding of maternal DHA equilibrium at an RBC-DHA of 8 g% is in line with the optimal RBC-DHA status that has been suggested for the lowest risk of cardiovascular and psychiatric diseases, and thereby adds to the contention that *homo sapiens* has evolved in a land–water ecosystem.

7. DHA and AA are synergistic at low postpartum DHA status and antagonistic at high DHA status

The relationship between DHA and AA has been subject to many investigations and both synergistic [89–92] and antagonistic relations [93,94] have been reported. Horrobin et al. [95] were the first to note a synergistic relation between EPA and AA at a low administered EPA dosage and an antagonistic relationship between EPA and AA at high EPA dosage [95]. We explored this relationship in our data from Tanzania and found synergism between DHA and AA at low DHA status and antagonism at high

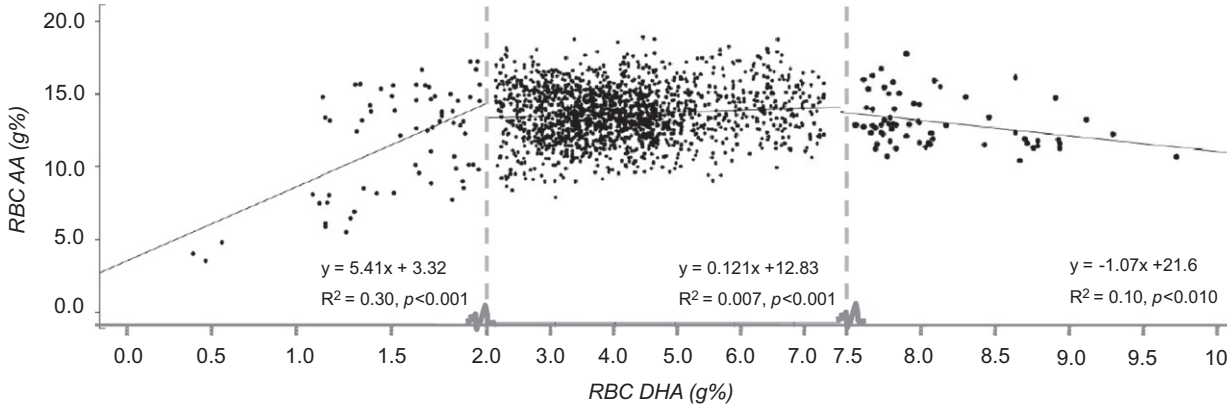

Fig. 6. The relation between RBC-DHA and RBC-AA for 1866 infants, males and pregnant and non-pregnant females. Note the different scales for RBC-DHA $<$2 and $>$7.5 g%.

DHA status [49]. Synergism/antagonism was also found in our dataset of 890 umbilical veins and arteries and in our dataset of RBC-FA deriving from 1866 infants, males and pregnant and non-pregnant females (Fig. 6) [96]. Synergism/antagonism between DHA and AA seems therefore not limited to pregnancy and lactation but occurs throughout the entire life cycle. As suggested by Horrobin et al. [95], optimum health may require raising both ω3 and ω6 fatty acids from low status and it is conceivable that synergism/antagonism actually aims at a certain balance between LCPω3 and LCPω6. We recently estimated that our hunting–gathering ancestors living in a water–land ecosystem had daily intakes of gram amounts of AA, EPA and DHA [7], which contrasts with the current daily (French) intakes of about 200 mg AA and 275 mg DHA (men) from a typically Western diet [97]. It is in this respect of importance to note that the above noted seemingly optimal RBC-DHA levels of >8 g% [81–85] reside in the antagonistic area of the bell-shaped DHA–AA relation (Fig. 6). This suggests that an antagonistic relation between DHA and AA might have been the physiological standard for human beings and that a high DHA intake is necessary to keep AA levels in check, possibly to maintain the balance between the proinflammatory and anti-inflammatory metabolites of AA, EPA and DHA [1].

8. Merging intrauterine biomagnification/attenuation and postnatal synergism/antagonism

We suggest that the intrauterine DHA biomagnification noted in mothers with low fish intakes aims at a synergistic increase of fetal DHA status to maintain a balance with the much easier formed AA. The subsequent bioattenuation at higher DHA status, as occurring in mothers with high fish intakes, may on its turn prevent abundant passage of DHA across the placenta, and thereby an antagonistic decrease of fetal AA status in competition-sensitive fetal organs. Such a barrier might be important since AA is implicated in fetal growth [12,18,55,56] and rapidly accretes in the fetal brain [16–20,57]. With increasing gestation, DHA becomes increasingly important for neurodevelopment and even more so after birth [12,18,88]. The postnatal DHA surge via the milk may therefore be regarded as a form of postnatal biomagnification, but this surge is unable to prevent a postnatal RBC-DHA drop in infants born to mothers with low and intermediate fish intakes. Analogous to the intrauterine period, the resulting low DHA status in infants born to women with low fish intakes might have synergistically lowered their RBC-AA, while the high DHA status of the infants born to mothers with high fish intakes might have lowered their RBC-AA in an antagonistic manner. We suggest that the intrauterine regulation of DHA status via biomagnification/attenuation is likely to conserve the important role of AA in the developing infant during pregnancy, while the postnatal DHA surge via the milk aims at the suppression of AA in an antagonistic manner.

9. Conclusions

Our data indicate that fetal AA status is high and tightly regulated, probably to support adequate fetal growth and neurological development. Biomagnification of DHA across the placenta occurs at the expense of the mother and may aim at a synergistic increase of fetal AA and DHA status. Bioattenuation of DHA during pregnancy may on the other hand aim at the prevention of competition of DHA with AA in the fetus at high maternal fish intakes. A maternal RBC-DHA of 6 g% seems sufficient to maintain a constant infant DHA status during pregnancy and notably lactation, but a maternal RBC-DHA of at least 8 g% is needed to prevent maternal DHA depletion notably during lactation. The latter DHA status concurs with the lowest risks of cardiovascular and psychiatric diseases in adults. Taken together, these data and also the high intakes of LCPω3 and LCPω6 from the presumed diet of our Paleolithic ancestors suggest that bio-attenuation of DHA during pregnancy and postnatal antagonism of AA status by dietary DHA are the physiological standard for human beings across the life cycle.

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